

WE CLAIM:

1. A method for detecting a mismatch in a test double stranded nucleic acid target, comprising

- a) contacting the target with
 - i) a Mu-end nucleic acid, and
 - ii) a phage Mu transposase,

under conditions effective for the Mu-end nucleic acid to transpose into the target at about the site of a mismatch, if the target comprises a mismatch, and

b) detecting transposition of the Mu-end nucleic acid into the target, wherein transposition of the Mu-end nucleic acid into the target at a predominant site indicates the presence of a mismatch at about that site.

2. The method of claim 1, wherein the Mu-end nucleic acid is detectable.

3. The method of claim 2, wherein the Mu-end nucleic acid is detectably labeled.

4. The method of claim 1, wherein the target nucleic acid is detectably labeled.

5. The method of claim 1, wherein the target and/or the Mu-end nucleic acid are DNA.

6. The method of claim 1, wherein the target is generated by PCR.

7. The method of claim 1, further comprising

c) contacting a control duplex nucleic acid, comparable to the test double stranded nucleic acid target, but known to be free from mismatches, with

- i) a Mu-end nucleic acid, and
- ii) a phage Mu transposase,

under conditions effective for the Mu-end nucleic acid to transpose into the control duplex at about the site of a mismatch, if the control duplex comprises a mismatch,

d) detecting transposition of the Mu-end DNA into the control duplex, and
e) comparing the transposition of the Mu-end nucleic acid into the test target and into the control duplex,

wherein an increased incidence of transposition of the Mu-end nucleic acid into the test target at a predominant site compared to the incidence of transposition of the Mu-end nucleic acid into the control duplex at the corresponding site indicates the presence of a mismatch at that site in the test target.

8. The method of claim 7, wherein the detection and comparing comprise
 - i) separating by size the products of the transposition reaction, and
 - ii) comparing the amount and sizes of the products from the treated test target with the products from the treated control duplex, as an indication of the presence or absence of a mismatch in the test target.
9. The method of claim 1, wherein the mismatch indicates the presence of a mutation.
10. The method of claim 1, wherein the mismatch indicates the presence of a polymorphism.
11. The method of claim 1, which is a method for typing a pathogenic microorganism strain.
12. The method of claim 1, which is a high throughput method.
13. The method of claim 1, which further comprises determining the location of the mismatch,

wherein the transposition comprises nicking one strand of the target at about the site of the mismatch and ligating the 3' terminus of the proximal end of the Mu-end nucleic acid to the 5' terminus of the nicked target strand, thereby generating four transposition targets, further comprising determining the length of one or more of the transposition products, wherein the length of one or more of the transposition products indicates the site of the mismatch.
14. A method for detecting the presence of a mutation or polymorphism in a nucleic acid of interest, comprising

a) generating a double stranded nucleic acid target having a first strand and a second strand, wherein the first strand comprises a portion of the nucleic acid of interest, which may contain the mutation or polymorphism, and the second strand comprises a comparable portion of a wild type nucleic acid,

- b) contacting the double stranded nucleic acid target with
 - i) a Mu-end nucleic acid, and
 - ii) a phage Mu transposase,

under conditions effective for the Mu-end nucleic acid to transpose into the target at about the site of a mismatch, if the target comprises a mismatch, and

- c) detecting transposition of the Mu-end DNA into the target,
wherein transposition of the Mu-end nucleic acid into the target at a predominant site indicates the presence of a mutation or a polymorphism in the nucleic acid of interest.

15. The method of claim 14, wherein the nucleic acid of interest comprises a mutation which is diagnostic of a disease or a condition, or a susceptibility to the disease or condition.

16. The method of claim 14, wherein the nucleic acid of interest comprises a polymorphism.

17. The method of claim 14, wherein the nucleic acid of interest comprises a mutation that is in an essential gene.

18. The method of claim 14, wherein the nucleic acid of interest comprises a mutation in a CFTR, APC, p53, Rb, BRCA1, HMSH1, or HMLH1 gene.

19. The method of claim 14, which is a method for screening an embryo for the presence of a mutation.

20. The method of claim 14, which is a method for detecting the presence of a known mutation in a gene of interest.

21. The method of claim 14, which is a method for detecting the presence of a previously unidentified mutation in a gene of interest.

22. The method of claim 14, which is a method for diagnosing the presence or absence of a tumor-promoting mutation.

23. The method of claim 14, which further comprises determining the location of the mutation or polymorphism in the nucleic acid of interest,

wherein the transposition comprises nicking one strand of the target at about the site of the mismatch and ligating the 3' terminus of the proximal end of the Mu-end nucleic acid to the 5' terminus of the nicked target strand, thereby generating four transposition targets,

further comprising determining the length of one or more of the transposition products,

wherein the length of one or more of the transposition products indicates the site of the mismatch.

24. The method of claim 23, wherein the determining of the length of the transposition products is achieved by separating the transposition products by size.

25. The method of claim 24, wherein the size separation is performed by electrophoresis.

26. The method of claim 25, wherein herein the electrophoresis is on an acrylamide gel, an agarose gel, or in a capillary tube.

27. The method of claim 23, further wherein, following step b), the product(s) of the transposition reaction are amplified using one Mu end specific primer and one primer specific to a region of interest from the target nucleic acid.

28. A method of detecting the presence and location of a mutation or polymorphism in a DNA of interest, comprising

- a) amplifying by PCR a portion of the DNA of interest suspected of containing the mutation or polymorphism and, optionally, co-amplifying the same portion of a comparable control DNA which lacks any mutation within that portion, to form a duplex,
- b) contacting the duplex with
 - i) a Mu-end nucleic acid, and
 - ii) a phage Mu transposase,

under conditions effective for the Mu-end nucleic acid to transpose into the duplex at about the site of a mismatch, if the duplex comprises a mismatch,

- c) separating by size the products of the transposition reaction, and
- d) determining the amount and size of the transposition product(s),

wherein transposition of the Mu-end nucleic acid into the duplex at a predominant site indicates the presence of a mutation in the nucleic acid of interest, and

wherein the size of the transposition product(s) indicates the site of the mutation, and

wherein the presence of a predominant site of Mu-end DNA integration when the DNA of interest is subjected to PCR in the absence of the control DNA indicates that the DNA of interest is heterozygous for the mutation, and

wherein the presence of a predominant site of Mu-end DNA integration only when the DNA of interest is co-amplified by PCR in the presence of the control DNA indicates that the DNA of interest is homozygous for the mutation.

29. The method of claim 28, wherein the size separation is performed by electrophoresis.

30. The method of claim 29, wherein herein the electrophoresis is on an acrylamide gel, an agarose gel, or in a capillary tube.

31. The method of claim 28, further wherein, following step b), the product(s) of the transposition reaction are amplified using one Mu end specific primer and one primer specific to a region of interest from the target nucleic acid.

32. An *in vitro* reaction mixture comprising

- a) a Mu-end nucleic acid,
- b) a phage Mu transposase, and
- c) a double stranded target DNA comprising a mismatch.

33. A kit for determining if a double stranded nucleic acid target of interest contains a mismatch, comprising

- a) a Mu-end nucleic acid,
- b) a phage Mu transposase, and

c) means for determining if the Mu-end nucleic acid transposes into the target at a predominant site and/or

d) instructions for determining if the double stranded nucleic acid target contains a mismatch,

and, optionally, further comprising,

e) oligonucleotide primers suitable for amplification of a nucleic acid fragment comprising a portion suspected of containing a mutation, and/or

f) means for labeling the Mu-end nucleic acid, and/or

g) a preformed gel.

34. The kit of claim 33, wherein the Mu-end nucleic acid and the phage Mu transposase are in a pre-assembled mixture.

35. The kit of claim 33 or claim 34, which is for detecting the presence of a mutation or polymorphism of interest in a nucleic acid molecule.

36. A method for detecting a mismatch in a double stranded nucleic acid target, comprising

a) contacting the target with

i) a D108-end nucleic acid, and

ii) a phage D108 transposase,

under conditions effective for the D108-end nucleic acid to transpose into the target at about the site of a mismatch, if the target comprises a mismatch, and

b) detecting transposition of the D108-end DNA into the target,

wherein transposition of the D108-end nucleic acid into the target at a predominant site indicates the presence of a mismatch at about that site.